Use of quantitative immunohistochemistry to evaluate marker expression in breast cancer

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Abstract

Breast cancer is a heterogenous disease and there is a great need for further individualized treatment. Due to extensive intertumor and intratumor heterogeneity, immunohistochemistry provides valuable spatially resolved marker analysis at the tissue level. Pathologists typically evaluate protein marker expression visually in formalin-fixed paraffin-embedded tumor sections by chromogenic immunohistochemistry. However, pathologist scoring of chromogen staining intensity is subjective and provides only reduced data that is discrete, either ordinal (e.g. 1, 2, 3) or nominal (negative/positive). In contrast, emerging digital pathology platforms allow quantification of chromogen or fluorescence signals by computer-assisted image analysis, providing continuous signal intensity values. Fluorescence-based immunohistochemistry (IF-IHC) provides greater dynamic signal range than chromogen-immunohistochemistry. Combined with image analysis software, fluorescencebased immunohistochemistry holds potential for enhanced sensitivity and greater analytic resolution resulting in more robust quantification. However, commercial fluorescence scanners and image analysis software differ in features and capabilities. Vendors' claims of objective quantitative immunohistochemistry are difficult to validate since pathologist scoring is subjective and, importantly, there is no accepted gold standard to measure against. We will present validation studies and progress with quantitative immunohistochemistry on large cohorts of breast cancer using different technologies. The path towards implementation of objective tumor marker quantification in pathology laboratories will be discussed.

Biography

Hallgeir Rui is a PhD holder and serves as the WBCS Endowed Professor of Breast Cancer Research in the Department of Pathology at the Medical College of Wisconsin, Milwaukee, WI. He has previously held positions at Thomas Jefferson University, Philadelphia, PA, Georgetown University, Washington DC, and Uniformed Services University, Bethesda, MD. He completed his Post-doctoral training at NCI, Frederick, MD and Moffitt Cancer Center, Tampa, FL. He received his MD and PhD degrees at the University of Oslo, Norway. His laboratory research is centered on analyses of human breast cancer to improve tailored therapy.